REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 1-28 are in the case.

I. ELECTION/RESTRICTION

The election of Group II is hereby affirmed. The remaining claims have been retained in the case as it is believed that such claims can coexist in the present application with the elected claims. Reconsideration and rejoinder of all of the claims in this are accordingly respectfully requested.

II. SEQUENCE LISTING

Corrected sequence listing materials have been submitted on October 15, 2003. It is believed that the sequence listing requirements for this application are now in compliance with the regulations.

III. THE 35 U.S.C. §112, SECOND PARAGRAPH, REJECTION

Claims 2-15 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for the reasons detailed on pages 3 and 4 of the Action. In response, and without conceding to the merit of this rejection, the claims have been amended to deal with the formal points raised by the Examiner.

Claim 2 has been amended by reciting positively that the enzyme is a translocating enzyme and by deleting "capable of" at line 3. Claim 2 has also been amended by deleting the first occurrence of the term "during the translocation". Claim 12 has been amended to be in conformity with amended claim 2.

In the molecular motor system according to the instant invention, cleavage of the nucleic acid does not occur. Even in prior art systems, where cleavage is permitted, such cleavage does not occur "during" the translocation. Cleavage will only occur if the translocation process is stalled or altered in some way, or reaches its natural conclusion. The revised claim language makes it clear that cleavage is actually prohibited from occurring at all.

Claim 10 has been amended by effectively splitting that claim into a number of simpler claims. The expression "means for binding" defines the situation in which an object to be translocated is incapable of binding to the distal region of the nucleic acid. In such circumstances, an intermediary is used which is capable of binding to the distal region of the nucleic aid, but which is also capable of binding to the object. Hence, the object becomes bound to the distal region of the nucleic acid by indirect means of attachment. In the instant specification, an example of the object used is a magnetic particle. The magnetic particle is coated with streptavidin and the distal end of the nucleic acid is provided with a "linker" or "binding ligand" of biotin. The strong affinity of streptavidin for biotin enables the magnetic particle to be indirectly attached to the distal end of the nucleic acid through the intermediary of the biotin. Hence, the "bound" substance is biotin. When the molecular motor system is activated and the biotin is translocated, the indirectly-attached magnetic particle is also translocated. The facility for direct or indirect attachment of an object allows for an intermediate type of molecular motor system to be defined, namely one in which the distal end of the nucleic acid is provided with a linker but with no "object" associated with the linker.

New claim 29 defines a molecular motor system bound directly or indirectly to a

solid support. New claim 30 defines a molecular motor system in which the means of attachment between the nucleic acid/enzyme complex and a substance which is required to be translocated is either direct or indirect. New claims 30, 31 and 32 define particular variants thereof.

In light of the above, withdrawal of the outstanding 35 U.S.C. §112, second paragraph, rejection is now believed to be in order. Such action is respectfully requested.

IV. THE ANTICIPATION REJECTIONS

Claims 2-15 stand rejected under 35 U.S.C. §102(a) as allegedly anticipated by Janscak et al (1998). Claims 2, 3 and 7-12 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Yin et al. Claims 2-15 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Janscak et al (1996). Claims 2-15 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Mernagh et al. Those rejections are respectfully traversed.

For convenience in the discussion which follows, reference is made to the cited art as follows:

D1 - Janscak et al (Nucleic Acid Research, 1968, Volume 26, No. 19, pages 4439-4445)

D2 - Yin et al (Science, 1995, Volume 270, pages 1653-1657)

D3 - Janscak et al (Journal of Molecular Biology, 1996, Volume 257, pages 977-991)

D4 - Mernagh et al (Biological Chemistry, Volume 379, pages 497-503)

The Examiner will note that, in papers D1, D3 and D4, Keith Firman is named as a co-author. Dr. Firman is the named inventor in the present application.

The Applicant respectfully disagrees with the Examiner's art-based objections. D3, which is the earliest paper by Dr. Firman and his co-workers under present consideration, inaccurately reports the stoichiometry of the Type IC R-M enzymes studied. For this reason, it is perhaps not surprising that the Examiner may have misunderstood that reference. The stoichiometry of $R_1M_2S_1$ for the endonuclease suggested on page 980 of D3 was later shown to be incorrect and is reported as such in D1 and D4 (See D1, page 4439, right hand column: "The stoichiometry of this endonuclease preparation appeared to be $R_1M_2S_1$" (Emphasis added), and page 4440, first complete paragraph, first sentence: "In this paper we show that the purified EcoR124I restriction endonuclease is a mixture of two species, which have a sub-unit stoichiometry of $R_2M_2S_1$ and $R_1M_2S_1$, respectively. "See D4, page 497, right hand column: "the EcoR124I endonuclease has been reported to exist in the form R_1M_2S ...", and page 498, right hand column: "The SPR results are consistent with the formation of both R_1M_2S and R_2M_2S in a concentration dependant manner".

Also, the predicted stoichiometry of $R_1M_2S_1$ on page 980 of D3 was suggested for the native enzyme, which is known to cleave DNA.

There is no disclosure in D1, D3 or D4 of the isolated R_1M_2S species. By "isolated" in this context is meant separated in a form which can be harnessed to do useful work as a molecular motor, rather than merely isolated for the purposes of identification and characterization.

Since the references do not disclose the isolated R_1-complex, they might only be

relevant in regard to use of the native enzyme. However, the native enzyme is now known to be an equilibrium mixture of the R_1- and R_2- species and, as such, will always be able to cleave DNA. Use of the native enzyme therefore falls outside the scope of the present claims.

The Examiner asserts that the abstract of D1 discloses linear DNA-protein (enzyme?) complexes that translocate bound plasmids into an unmodified host cell. It is Applicant's position that this is a misinterpretation of the disclosure of D1. On page 4443, D1 discloses use of plasmid DNA for formation of the nucleic acid/enzyme complex. The plasmid DNA is cleaved to produce full-length linear DNA, but nowhere is it disclosed or suggested in D1 that the plasmid DNA is bound to a linear DNA-protein complex, as the Examiner alleges. None of the references D1, D3 or D4 discloses binding a substance other than the enzyme to DNA.

In light of the above, it is clear that none of the references D1, D3 or D4 discloses or suggests all of the elements defined in claim 2 as amended. In particular, none of D1, D3 or D4 discloses provision at a first, proximal region of a nucleic acid of a translocating enzyme that does not cleave the DNA, or the provision at a second, distal region of the nucleic acid of a substance bound to the nucleic acid that becomes translocated as a result of the nucleic acid translocation. Withdrawal of the anticipation rejections based on those references is accordingly respectfully requested.

Reference D2 discloses a molecular motor which operates in a different way from the molecular motor of the present invention. Figure 1 on page 1654 of D2 illustrates a molecular motor typical of prior art systems. In particular, with reference to views (A) and (B), it can be seen that the enzyme (RNA polymerase) travels along the DNA,

bringing the distal end closer to the polymerase binding site, but allowing the original binding site to recede in the opposite direction. By contrast, the molecular motor according to the claimed invention remains fixed to the nucleic acid at the (original) binding site. When the motor is activated, the distal end of the nucleic acid is brought closer to the binding site, but there is no movement of the proximal end of the nucleic acid relative to the enzyme.

To assist in further in understanding the differences between the present invention and the disclosure of D2, the Examiner's attention is directed to the attached document entitled "Molecular Motor Explanation" provided by the inventor. An animation is available on the Internet at:

www.nanonet.org.uk/nanotechnology.asp

In light of the above, it is clear that none of the cited references anticipates the presently claimed invention. Reconsideration and withdrawal of all of the outstanding anticipation rejections are accordingly respectfully requested.

V. SPECIFICATION

The specification has been amended to include customary headings, including a brief description of the drawings.

Allowance of the application is awaited.

Respectfully submitted,

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US Patent Application from PCT Application PCT/GB00/02304
"A POLYNUCLEOTIDE MOTOR, A MOTOR SYSTEM, THEIR PREPARATION AND USES"
Applicant: FIRMAN, Keith

MOLECULAR MOTOR EXPLANATION

When the enzyme is merely complexed with the DNA, nothing happens. To power the molecular motor it is necessary to add some suitable "fuel", such as magnesium ions and ATP.

The "bound substance" is the thing which it is desired to move using the "molecular motor" action of the enzyme. To understand what is happening it is helpful to think of a "pull through" action. The DNA is like a piece of string having a knot in it, the knot being the place where the enzyme binds to it. The knot is slightly loose so that a free end of the piece of string can be pulled through the knot. Now, imagine that the free end has a knot in it. That second knot represents the point at which the "bound substance" is bound to the DNA. Again, the free end is pulled through the first knot, but this time, there is a limit as to how far it can be pulled: when the second knot comes up to the first knot, the free end can be pulled no further. The first knot is too tight to allow the second knot to be pulled through it. The process therefore comes to a stop. The overall result is that the second knot has moved relative to the first. In other words, the "bound substance" has moved relative to the stationary enzyme.

It is desirable to prevent the DNA from being cleaved during a cycle of the motor. This is achievable in type I endonucleases if the stoichiometry of the enzyme can be maintained at one unit of HsdR (restriction sub-unit) to two units of HsdM (modification of DNA by methylation) and one unit of HsdS (specificity of the restriction). This is abbreviated to $R_1M_2S_1$.

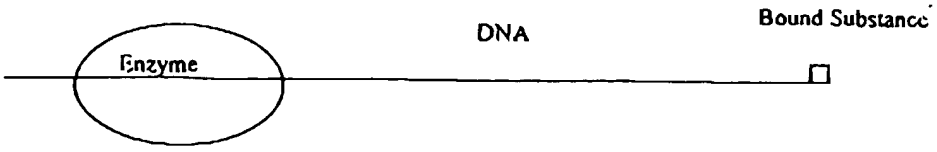
Thus, continuing with the analogy, the string remains uncut after the pulling action has been stopped by the second knot. No scissors or knife cut the string.

It is important to remember that the enzyme is bound to the DNA. That is, it is stationary. This is in contrast to polymerases which move along the DNA.

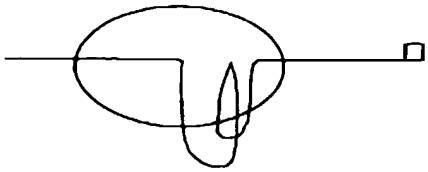
The following sketch will assist understanding.

Molecular motor sketch

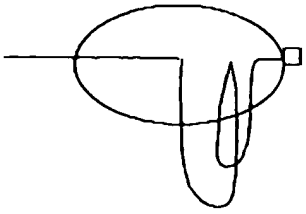
1.



2.



3.



Until the concept of the molecular motor was realised by the present invention, there was no reason for anyone to bind a substance to the enzyme-DNA complex.

In the invention, the enzyme-DNA complex may have a solid support attached to the nucleic acid (without necessarily having the "bound substance" attached as well).

In one aspect, the molecular motor can be considered as a "fishing rod". By binding the nucleic acid at some point to a solid phase, substances present in solution can be fished out. They may be, for example, DNA molecules which hybridise to nucleic acid sequences present in the enzyme-nucleic acid complex.